for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

SHANKS & HERBERT

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MARKED-UP VERSION OF THE AMENDMENTS

In the Specification:

On page 17, please replace the paragraph in lines 10-19 with the following paragraph:

FIG. 1. Schematic diagram of gene activation events described herein. The activation construct is transfected into cells and allowed to integrate into the host cell chromosomes at DNA breaks. If breakage occurs upstream of a gene of interest (e.g., Epo), and the appropriate activation construct integrates at the break such that its regulatory sequence becomes operably linked to the gene of interest, activation of the gene will occur. Transcription and splicing produce a chimeric RNA molecule containing exonic sequences from the activation construct and from the endogenous gene. Subsequent translation will result in the production of the protein of interest. Following isolation of the recombinant cell, gene expression can be further enhanced via gene amplification. The polyA tail is set forth in SEQ ID NO:33.

On page 21, please replace the paragraph in lines 6-17 with the following paragraph:

FIG. 13. Illustration depicting two transcripts produced from the integrated vectors described in Figures 12A-12G. DNA strands are depicted as horizontal lines. Vector DNA is shown as a black line. Endogenous genomic DNA is shown as a grey line. Rectangles depict exons. Vector-encoded exons are shown as open rectangles, while endogenous exons are shown as shaded boxes. S/D denotes a splice donor site.

Following integration, the vector encoded promoters activate transcription of the endogenous gene. Transcription resulting from the upstream promoter produces a spliced RNA molecule containing the vector encoded exon joined to the second and subsequent exons from an endogenous gene. Transcription from the downstream promoter, on the other hand, produces a transcript containing the sequences downstream of the integrated DNA joined to exon I and the subsequent exons from an endogenous gene. The polyA tails are set forth in SEQ ID NO:33.

On page 26, please replace the paragraph in lines 6-25 with the following paragraph:

FIG. 23A-23D. Example of a multi-Promoter/Activation Exon Vector. Each vector is illustrated schematically in its linearized form. Each horizontal line represents a DNA molecule. The arrows denote promoter sequences. Boxes indicate exons. Hatched boxes indicate untranslated regions. It is understood that the exons on these vectors may be untranslated, or may contain a start codon and additional codons as described herein. The following designations were used: splice donor site (S/D), vector promoter #1 (VP #1), vector promoter #2 (VP #2), vector promoter #3 (VP #3), and vector promoter #4 (VP #4). Individual vector activation exons are designated A, B, C, and D (SEQ ID NOS: 29-32, respectively). Each activation exon may contain a different structure. The structure of each activation exon and its flanking intron are shown below. It is understood, however, that any activation exon described herein, may be used on these vectors, in any combination and/or order, including exons that encode signal sequences,

partial signal sequences, epitope tags, proteins, portions of proteins, and protein motifs. Any of the exons may lack a start codon. In addition, while not illustrated in these examples, these vectors may contain a selectable marker and/or an amplifiable marker. The selectable marker may contain a poly (A) signal or a splice donor site. When present, the splice donor site may be located upstream or downstream of the selectable marker. Alternatively, the selectable marker may not be operably linked to a poly (A) signal and/or a splice donor site.

On page 30, please replace the sentence on line 9 with the following sentence:

FIG. 37A-37C. Nucleotide sequence of pRIG-T (SEQ ID NO:28).

62. (Once amended) A method for drug discovery comprising:

(a) integrating a vector into the genome of one or more eukaryotic cells, wherein said vector integration activates expression of an endogenous gene in said one or more cells;

(b) culturing said one or more cells under conditions favoring expression of said activated gene, thereby producing a gene product of said activated gene;

(c) screening said one or more cells for a cell in which a desired gene is activated or for a cell in which a desired phenotype is induced by said activated gene;

(d) treating said cell, in which said desired gene is activated or in which said desired phenotype is induced, with one or more test compounds to be screened for drug activity; and

(e) determining the ability of said one or more test compounds to interact with a product of said desired activated gene.

63. A method for drug discovery comprising:

(a) integrating a vector into the genome of one or more eukaryotic cells, wherein said vector integration activates expression of an endogenous gene in said one or more cells;

(b) culturing said one or more cells in reduced-serum cell culture medium under conditions favoring production of a protein encoded by said activated gene and secretion of said protein into the cell culture medium;

(c) screening said one or more cells for a cell in which a desired gene is activated and the protein encoded by said desired gene is secreted into the cell culture medium; and

(d) screening one or more test compounds for drug activity by determining the ability of said test compounds to interact with said secreted protein in said cell culture medium.

64. The method of claim 63, further comprising concentrating said cell culture medium prior to said screening in (d).

65. The method of claim 63, further comprising isolating said protein prior to said screening in (d).

66. The method of claim 62 wherein said vector comprises a transcriptional regulatory sequence and wherein expression of said endogenous gene is activated by means of said transcriptional regulatory sequence.

67. The method of claim 63 wherein said vector comprises a transcriptional regulatory sequence and wherein expression of said endogenous gene is activated by means of said transcriptional regulatory sequence.

68. The method of any of claims 62–67 wherein said vector integrates into the genome by non-homologous recombination.

69. (New) A method for drug discovery comprising:

(a) integrating a vector, comprising a promoter, into the genome of one or more eukaryotic cells, by non-homologous recombination, wherein said promoter activates expression of an endogenous gene in said one or more cells;

(b) culturing said one or more cells under conditions favoring expression of said activated gene, thereby producing a gene product of said activated gene;

(c) screening said one or more cells for a cell in which a desired gene is activated or for a cell in which a desired phenotype is induced by said activated gene;

(d) treating said cell, in which said desired gene is activated or in which said desired phenotype is induced, with one or more test compounds to be screened for drug activity; and

(e) determining the ability of said one or more test compounds to interact with a product of said desired activated gene or to affect said desired phenotype.